

## COMMENTARY

## CONFLICT OF INTEREST

The authors state no conflict of interest.

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## Some Light on the Photobiology of Vitamin D

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In this issue, Bogh *et al.* report a study that begins to address the important public health question of skin surface area and UVB exposure dose, related to erythema, necessary to achieve a given level of vitamin D status. They demonstrate the importance of baseline vitamin D status in conducting such studies. A smaller substudy suggests that skin pigment is not a barrier to vitamin D photosynthesis.

*Journal of Investigative Dermatology* (2010) **130**, 346–348. doi:10.1038/jid.2009.419

### Introduction

The benefits of vitamin D and how best to obtain and maintain optimal levels are highly controversial topics that have enormous potential implications for human health. Nature has provided humans with two sources of vitamin D: solar UVB radiation and diet. However, most foods provide very little vitamin D, especially in typical Western diets. The exception is oily fish. Manmade interventions include food fortification in some countries, supplementation, and the use of tanning devices with UVB. Any discussion on vitamin D status should be based on facts. There is a surprising lack of careful, published investigation (as opposed to observation/extrapolation/calculation) into the photobiology of vitamin D *in vivo* and its interaction with skin color. Furthermore, there is a lack of data that compare the effects of UVR with other approaches to maintaining vitamin D

status performed in the same laboratories to minimize experimental variation.

### The significance of this study

The study by Bogh *et al.* (2010, this issue) is a welcome and timely addition to our knowledge in the photobiology field. The baseline data show that 85% of 182 people screened for the study were either vitamin D (25(OH)D) insufficient (67% < 50 nmol l<sup>-1</sup>) or deficient (18% < 25 nmol l<sup>-1</sup>) in Denmark at 56°N during the winter. The limitation of these definitions of vitamin D status is discussed in this issue's Editorial, by Reddy and Gilchrist (2010). The backs and chests of volunteers with skin types I–VI were exposed to three standard erythema doses (SEDs) of UVB for 4 days over 1 week. The UVB source used was very rich in the spectral region that converts 7-dehydrocholesterol to pre-vitamin D in the skin. The sites exposed represent

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~25% body surface area as estimated by the approach of Augustsson *et al.* (1992). It should be stressed that an SED is independent of personal UVR sensitivity and is a measure of erythral efficacy that is independent of source spectrum. A dose of 3 SEDs is equivalent to about 1 minimal erythema dose (MED) in skin types I/II and would be suberythemogenic (approximately 0.5 MED) in skin types III/IV (Harrison and Young, 2002). The authors show that baseline 25(OH)D is the determinant of the response to UVB exposure. The lower the baseline level, the greater the response, which supports homeostatic control. The regression line in Figure 3 in the article by Bogh *et al.* indicates that individuals in the insufficient/deficient baseline range had an increase of 20–30 nmol l<sup>-1</sup> 25(OH)D, a very substantial response, in about 1 week. This essentially brought people who were insufficient into sufficiency and those who were deficient into insufficiency. However, it must be stressed that a relatively large surface area was exposed, and, at least in skin types I/II, the exposure doses would have been approximately erythemogenic.

The UVR doses used in the study by Bogh and co-workers should be placed into context. The same authors have performed several studies in which UVR exposure was measured over extended periods in different populations in spring/summer in Denmark (56°N) using time-stamped personal electronic dosimeters. In people working indoors without engaging in sun-seeking behavior, the median daily dose was 0.3 SED (range: 0–3.9) on working days and 0.6 SED (range: 0.1–3.5 SED) on their days off (Thieden *et al.*, 2004). The measurements were taken on subjects' wrists, and it is estimated that the dose to the face is two-fold greater. Thus, the doses used in Bogh and colleagues' study were 5–10 times higher than median wrist exposures at the same latitude. Not surprisingly, higher daily exposures have been measured in Queensland, Australia, with, for example, home workers in Brisbane (27.4°S) having weekday shoulder exposure medians of 2.0–8.0 SEDs, depending on the time of year. Outdoor workers at the same latitude showed values of 3.0–10.0 SEDs (Parisi *et al.*, 2000). It has been estimated that the average American is

## Clinical Implications

- Baseline 25(OH)D is a determinant of UVB-induced vitamin D synthesis.
- Vitamin D photosynthesis is independent of skin pigmentation for a fixed UVB dose and similar baseline 25(OH)D level.
- Is adventitious solar exposure of face and hands sufficient to maintain vitamin status?

exposed to about 250 SEDs per working year, mostly in the spring and summer (Godar *et al.*, 2001). This can be increased by 78 SEDs (i.e., about 30%) with a 3-week vacation (i.e., by 3.7 SEDs per day). It is perhaps surprising that even studies in sunny climates have demonstrated suboptimal vitamin D status. This conundrum remains to be investigated and explained.

It is often said that short solar exposures to the face and the back of the hands are adequate to maintain optimal vitamin D status, but this does not seem to have been experimentally verified. Using the technique of Augustsson *et al.* (1992), this would be equivalent to ~10% of the body surface and would increase to ~20% if the lower arms are included, which is still less than the ~25% surface area in Bogh and colleagues' study. Whether this is sufficient with lower UVR doses, which are more typical of daily exposure at given latitudes, over a longer period of time, remains to be tested under laboratory and/or field conditions. In this context it should also be noted that an SED of solar UVR will be less effective at vitamin D synthesis than an SED from the very UVB-rich source used in this study. This is because UVA in sunlight makes a much greater contribution to erythema than with the source used by Bogh *et al.*

### Skin color and vitamin D synthesis

Of particular interest is the substudy on the effect of pigmentation (see Table 2 in the article by Bogh *et al.*) on vitamin D synthesis; people with darker skin tend to have suboptimal vitamin D status. Although the sample size is small ( $n = 9$  pairs matched with similar baseline 25(OH)D), the data indicate that skin type and measured pigmentation have no effect on the synthesis of vitamin D after exposure to the same fixed doses of UVB; this means that from an erythral (MED) point of view the

darker skin types, which included V and VI, had lower doses. This study should be confirmed with a larger sample size, and broadened in its remit, but it calls into question much of the dogma about the relationship between pigmentation and vitamin D status, and perhaps even the hypothesis that vitamin D was a major factor in the evolution of skin color (Yuen and Jablonski, 2009). However, the data of Bogh *et al.* are in contrast with those recently published by Armas *et al.* (2007) in a larger study. Armas *et al.* exposed 90% of the body surface area three times per week for 4 weeks. The doses given to skin types I/II would be expected to be in the MED range, and doses up to fourfold greater were given to individuals with darker skin types. The estimated increase of 25(OH)D in skin types I/II for a dose of 30 mJ/cm<sup>2</sup> over 4 weeks was comparable to that obtained in 1 week in Bogh and colleagues' study. Higher doses were required for darker skin types. Thus, overall, the outcomes of the two studies, with very different designs, are contradictory. However, it should be noted that the study population of Armas *et al.* (2007) indicated a relationship between skin color and baseline 25(OH)D, with higher values for fairer skin types. The current study shows that this difference in baseline 24(OH)D levels could have influenced the outcome.

### How best to obtain vitamin D

Some three decades ago, some studies compared daily UVR with daily vitamin D supplementation, at different doses, for 3 weeks in vitamin D-deficient/insufficient people (Stamp *et al.*, 1977). The UVR details are not comprehensive but would appear to be for whole-body exposure to a source with a peak at 290 nm. The initial "dose" was 1 minute, on dorsal and ventral surfaces, but this was increased by 1 minute each day, except when erythema was present (Stamp, 1975), indicating that the doses

were at the high end of suberythematous. This UVR protocol was equivalent to a vitamin D dose of 250 µg/day, which is 10,000 international units. A level of about ~100 nmol l<sup>-1</sup> was reached at 3 weeks, with about 70 nmol l<sup>-1</sup> reached in 2 weeks. This daily supplement dose is 10 times higher than that recommended by the US Department of Health and Human Services and the US Department of Agriculture (Johnson and Kimlin, 2006).

Much of the advice pertaining to "safe sun" is based on the prevention of erythema because it is a readily accessible clinical readout, and sunburn is a risk factor for malignant melanoma in susceptible skin types. It is possible to compare, in theory, the relative risks and benefits of solar exposure using action spectra (wavelength dependence) for erythema and the synthesis of pre-vitamin D (not 25(OH)D) as biological weighting functions with solar spectra with different UVB/UVA ratios. The amount of UVB increases with the height of the sun, which is dependent on latitude, season, and time of day. Such calculations indicate that the optimal benefit-to-risk ratio occurs when the sun is high in the sky (Sayre and Dowdy, 2007), which is when people are advised to avoid the sun (e.g., about noon). These calculations are based on action spectra, which are likely to have large margins of error, and it would be desirable to test these results under field or laboratory conditions using 25(OH)D as the readout.

### Conclusions

The dermatology community is very mindful of the well-established detrimental effects of UVB. The community is increasingly aware of the role of UVB in vitamin D synthesis but is still skeptical of many of the health benefits attributed to vitamin D. Researchers are justifiably concerned about the misuse of information for financial gain or the inadvertent promotion of sun-seeking/tanning behavior. However, much work remains to be done in risk-versus-benefit assessment of UVR exposure, which will depend on a range of individual/demographic/cultural/geographic factors and on the communication of research outcomes and advice to the public. There is a clear need for a much better

understanding of the relationship among UVR spectrum, skin area and exposure dose, skin color, tanning, photoprotection, and vitamin D outcome. Some of these issues in the context of risk/benefit are currently being investigated in a multinational European Community-funded project, "ICEPURE: The Impact of Climatic and Environmental Factors on Personal Ultraviolet Radiation Exposure and Human Health" (see <http://www.icepure.eu> for details). Furthermore, we need a much better understanding of the relationship between the maintenance of vitamin D status by UVB versus diet/supplementation and their interactions.

### CONFLICT OF INTEREST

The author states no conflict of interest.

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## Cutaneous T-Cell Lymphoma: Two Faces of the Same Coin

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Primary cutaneous anaplastic large-cell lymphoma (C-ALCL) and cutaneous peripheral T-cell lymphoma not otherwise specified (C-PTL-NOS) are cutaneous T-cell lymphomas with distinct clinical behaviors. Whereas C-ALCL has a favorable prognosis with frequent spontaneous disease regression, C-PTL-NOS runs a more aggressive course. The molecular pathogenesis of these cutaneous T-cell lymphoma types has not yet been studied in detail. In this issue, van Kester *et al.* report new imbalances that could contribute to our understanding of the differences between these two lymphoma types.

*Journal of Investigative Dermatology* (2010) 130, 348–351. doi:10.1038/jid.2009.373

Cutaneous T-cell lymphomas (CTCLs) are non-Hodgkin's lymphomas char-

acterized by the clonal proliferation of skin-homing mature T lymphocytes. The

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